Docket No.: 248573US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:
Hiroshi HAGINO

GROUP: 1655

SERIAL NO: 10/771,527

EXAMINER: P. A. Leith

FILED: February 5, 2004

FOR: VASODILATOR PHARMACEUTICAL PREPARATION AND HEALTH FOOD COMPOSITION

DECLARATION UNDER 37 C.F.R. 1.132

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Sir:

Now comes Hiroshi Hagino who deposes and states that:

1. I am a graduate of Tokyo University and received my Doctorate of Agriculture degree in the year 1975.

2. I have been employed by SHIRAKO CO, LTD. for 7 years as a biochemist in the field of biochemistry.

3. I attest that the following experimental data is true and accurate (Please note: four figures (Figs. I-IV) are attached with the declaration).

Experiments in Rats

A peptide composition, in the form of a powder, comprising as an active ingredient peptides obtained by hydrolyzing proteins derived from laver, was obtained by decomposing proteins from laver (protein content is 40%) with the digestive enzyme pepsin. The thus digested sample was purified by absorption onto a cation exchange resin, followed by elution with a solution of aqueous ammonia. The portion of the eluted solution which comprised a high peptide content was collected, concentrated, and freeze dried to obtain a powder. The powder had a peptide content of 90-92%.

The powder was administered to rats as follows: Before administration of the powder (in the form of an aqueous solution) five-week old, Wister, male rats were fasted for 2 hours.

The powder was dissolved to form an aqueous solution (final concentration: 300 mg/ml), and was subsequently administered to the rats through a stomach sonde. As controls, a 4% sodium chloride solution and, separately, a placebo were also administered to rats.

The dose of the peptide composition administered to the rats was 300 mg/100g of body weight.

Attached Figure I shows that, over a 60 minute time period, with data points taken every 10 minutes (and averaged), both the placebo (line with squares) and the 4% sodium chloride solution (line with triangles) elicited no significant increase in blood flow. Conversely, the peptide composition achieved statistically significant increases in blood flow (line with circles) at the 40, 50, and 60 minute time points.

Blood flow was measured by a laser measuring machine for tissue-blood flow, FLO-NI type, made by the Omega Wave Company. To measure blood flow, the machine was set on the tail of a rat, laser light was then applied, and tissue-blood flow, as measured by the flow of red blood cells, was recorded by a light detector.

Attached Figure II shows that, over the same 60 minute time period, there was no observed hypotensive effect in the rats given the peptide composition. Blood pressure measurements describe the blood pressure both when the heart contracts (systolic) and when the heart relaxes (diastolic) and are given in measurements of systolic/diastolic mmHg (i.e., 120/80 mmHg). The systolic blood pressure (line with circles), at time points 35, 45, and 60 minutes, remained relatively constant at around 150 mmHg, showing a slight upward trend. Also, the diastolic blood pressure (line with squares) remained relatively constant at 100 mmHg at periods 30, 45, and 60 minutes.

Experiments in Humans

A peptide composition comprising, as an active ingredient, peptides obtained by hydrolyzing proteins derived from laver, was obtained as follows: Proteins in laver were

decomposed with the digestive enzyme, pepsin. The thus obtained peptides were subjected to spray drying to obtain a powder.

The powder was administered to each woman in the form of a water solution (total dose of powder = 3.2 g) by ingestion (drinking). Blood flow, body temperature, and blood pressure were measured, in the women, for 20 minutes before ingesting the composition and for 90 minutes after ingesting the composition.

Blood flow, in different areas of the body, was measured by a laser measuring machine (ALF 21RD).

As shown in attached Figure III, no hypotensive effect was observed, and the average systolic blood pressure of the women held constant at around 100 mmHg. Similarly, the average diastolic blood pressure of the women remained constant at around 60 mmHg for an average blood pressure reading of 100/60 mmHg.

As shown in attached Figure IV, there was a slight increase in blood flow in the skin of a finger and a significant increase in blood flow in the skin of a foot.

4. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

5. Further deponent saith not.

Signature

Mar. 24, 2006
Date

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